

# The Effect of Local Surface and Central Cooling on Adductor Pollicis Twitch Tension during Nitrous Oxide/Isoflurane and Nitrous Oxide/Fentanyl Anesthesia in Humans

Tom Heier, M.D.,\* James E. Caldwell, F.F.A.R.C.S.,† Daniel I. Sessler, M.D.,† Ronald D. Miller, M.D.‡

This study aimed to determine whether: 1) the method of cooling the hand (*i.e.* central [total body] vs. local surface [hand only]) influences the relationship between the adductor pollicis temperature and twitch tension; and 2) decreased evoked twitch response during hypothermia is due to reduced muscle temperature and/or the anesthetic drug used. First, the effect of local surface cooling on adductor pollicis twitch tension during isoflurane anesthesia was determined in 15 patients, while central body temperature was not allowed to decrease. Adductor pollicis temperature and twitch tension decreased in a linear manner ( $P < 0.05$ ). However, the magnitude of the decreased response was only 43% of that observed during central cooling in the authors' previous study under otherwise similar experimental conditions. Second, the effect of central cooling on adductor pollicis twitch tension during nitrous oxide/fentanyl anesthesia was determined in five patients. The twitch tension did not decrease until the adductor pollicis temperature decreased below 35.2° C. Below this temperature, twitch tension decreased 16%/° C reduction in muscle temperature. These results are similar to those obtained in the authors' previous study in patients anesthetized with nitrous oxide/isoflurane anesthesia. The authors conclude that both central and local surface cooling of the adductor pollicis muscle reduces twitch tension and that the decrease in adductor pollicis twitch tension is the same during nitrous oxide/isoflurane and nitrous oxide/fentanyl anesthesia. (Key words: Anesthetics, gases: nitrous oxide. Anesthetics, intravenous: fentanyl. Anesthetics, volatile: isoflurane. Muscle: force of contraction. Neuromuscular transmission: adductor pollicis twitch response. Temperature: adductor pollicis; central; skin.)

THE MECHANICAL RESPONSE of the adductor pollicis muscle to ulnar nerve stimulation is commonly used to assess neuromuscular function during anesthesia. In a previous study during nitrous oxide/isoflurane anesthesia, we defined a direct relationship between the adductor pollicis muscle temperature and twitch response when the temperature in that muscle was reduced secondary to central (total body) cooling.<sup>1</sup> The first aim of the present study was to determine whether the same relationship exists when the adductor pollicis muscle temperature is

reduced secondary to local surface (hand alone) cooling while the central temperature is not allowed to decrease.

In our previous study, patients were anesthetized with isoflurane, which may have contributed to the reduction in twitch tension.<sup>2-4</sup> We therefore tested the hypothesis that isoflurane, as opposed to central hypothermia, contributed to the observed decrease in twitch response. Thus, we repeated the experiment during nitrous oxide/fentanyl anesthesia, an anesthetic technique that has less influence on neuromuscular function.<sup>5</sup>

## Methods

With approval from our Committee on Human Research and written informed consent, we studied the twitch response in 20 unpremedicated ASA physical status 1 or 2 patients. The trachea of each patient was intubated without the aid of muscle relaxants in all patients. Ventilation was controlled to maintain end-tidal  $P_{CO_2}$  between 30 and 35 mmHg, as measured by mass spectrometry.

## PART I

Anesthesia was induced in 15 patients with thiopental 2-5 mg/kg iv and inhalation of isoflurane, 4-5% (inspired concentration), and was maintained with nitrous oxide 65-70%, and isoflurane 0.8-1.25% (end-tidal concentrations). A Grass® S88 nerve stimulator delivered supra-maximal square wave impulses of 0.2-ms duration in a train-of-four (TOF) sequence (2 Hz) via 27-gauge needle electrodes placed adjacent to the ulnar nerve at the wrist. Trains of stimuli were repeated at intervals of 15 s and the evoked mechanical response of the adductor pollicis muscle was quantified by a force-displacement transducer (Gould® Statham UTC3) and displayed on a polygraph. Adductor pollicis temperature was measured with a 22-gauge, 18-mm-long needle thermocouple (Mon-a-therm®, St. Louis, MO) placed directly into the muscle 1-cm distal to the metacarpophalangeal joint of the thumb. Central temperatures were measured using rectal or tympanic membrane thermocouples. These temperatures are similar to each other in patients not undergoing cardiopulmonary bypass.<sup>6</sup> The temperature of the skin overlying the thenar muscles was measured by a 1-cm-diameter, self-sticking thermocouple (Mon-a-therm®, St. Louis, MO). In five patients, an additional 8-mm-long needle

\* Visiting Assistant Professor, Department of Anesthesia.

† Assistant Professor of Anesthesia.

‡ Professor and Chairman, Department of Anesthesia, Professor of Pharmacology.

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Address reprint requests to Dr. Caldwell: Department of Anesthesia, University of California, Room S-436, San Francisco, California 94143-0648.

thermocouple was inserted beside the 18-mm-long muscle thermocouple to determine the temperature gradient between subcutaneous tissue and muscle. Central temperatures were maintained by covering the patients with blankets during induction of anesthesia, using active airway humidification, and low fresh gas flows in the anesthesia circuit. The operating room temperature was  $21 \pm 0.5^\circ\text{C}$  (mean  $\pm$  SD).

When muscle twitch tension and end-tidal gas concentrations had been stable for  $>20$  min, the thenar region of the monitored hand was cooled by placing ice cubes on the skin and blowing room-temperature air at the region using a Bair-Hugger<sup>®</sup> cooling/warming unit (Augustine Medical Inc<sup>®</sup>, Minneapolis, MN). When the maximum effect of local cooling was obtained, the thenar region was rewarmed by a stream of warm air ( $40^\circ\text{C}$ ) from the Bair-Hugger<sup>®</sup> unit.

**Statistical Analysis.** Willcoxon signed rank test was used to determine if significant changes in twitch tension and temperatures occurred during the experiment. Data obtained at the beginning and end of the cooling and of the rewarming period were compared for the following variables: adductor pollicis twitch tension, central adductor pollicis, subcutaneous tissue, and thenar skin temperatures.

To determine if there was a significant temperature gradient from thenar skin to the adductor pollicis muscle, thenar skin, subcutaneous, and muscle temperatures at the end of both the cooling and rewarming periods were compared using Kruskal-Wallis ANOVA and Mann-Whitney U test with Bonferroni correction for multiple comparisons.

Least-squares linear regression analysis was used to derive the relationship in each patient between adductor pollicis twitch tension and temperature during local surface cooling and rewarming. The decrease in twitch tension/ $^\circ\text{C}$  decrease in adductor pollicis temperature (average of individual regression slope values) during local surface cooling was compared with the value previously obtained under otherwise similar experimental conditions during central cooling using Mann-Whitney U test.<sup>1</sup>

Differences were considered statistically significant at  $P < 0.05$ .

## PART 2

Anesthesia was induced in five patients by iv administration of fentanyl 5–10  $\mu\text{g}/\text{kg}$  and thiopental 2–5  $\text{mg}/\text{kg}$  iv, and maintained with fentanyl infusion 2–6  $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$  and nitrous oxide 65–70%. Adductor pollicis twitch tension and temperatures were recorded using the technique described in part 1. Central temperature was maintained during induction of anesthesia. When muscle twitch tension and end-tidal gas concentrations

had been stable for  $>20$  min, central cooling was induced with lactated Ringer's solution ( $5\text{--}10^\circ\text{C}$ ), infused iv at a rate of 1 l/h into a vein in the arm opposite to the site of neuromuscular monitoring. Central temperatures were not allowed to decrease below  $34^\circ\text{C}$ . Room temperature was maintained between 19 and  $20^\circ\text{C}$ .

**Statistical Analysis.** The relationship between central and adductor pollicis muscle temperatures was derived by least squares linear regression analysis based on pooled data of all results.

Willcoxon signed rank test was used to determine if significant changes in temperatures and adductor pollicis twitch tension occurred during central cooling. Data obtained at the beginning and end of the cooling period were compared for the following variables: adductor pollicis twitch tension, and central and adductor pollicis temperatures. Data obtained in the present study were compared using Mann-Whitney U test with those obtained previously during nitrous oxide/isoflurane anesthesia.<sup>1</sup>

Assuming a precision of  $\pm 2\%$  for our system for recording twitch tension, we defined a value  $< 98\%$  of control as a decrease in twitch tension. For twitch tension values  $< 98\%$  of control we used least squares linear regression analysis to derive the relationship in each patient between adductor pollicis twitch tension and central and adductor pollicis muscle temperatures. The regression line was extrapolated back to a twitch tension of 100%, and the temperature at this point was defined as the threshold temperature at which twitch tension started to decrease.

Differences were considered statistically significant at  $P < 0.05$ .

## Results

In part 1, peripheral cooling during nitrous oxide/isoflurane anesthesia, the age of the patients was  $40 \pm 12$  yr (mean  $\pm$  SD) and their weight  $66 \pm 12$  kg (mean  $\pm$  SD). In part 2, central cooling during nitrous oxide/fentanyl anesthesia, the age of the patients was  $33 \pm 5$  yr (mean  $\pm$  SD) and their weight  $67 \pm 7$  kg (mean  $\pm$  SD). These numbers are not significantly different from those in the central cooling group in our previous study.<sup>1</sup>

## PART 1

The mean initial central, adductor pollicis, subcutaneous, and thenar skin temperatures were  $35.9 \pm 0.4$ ,  $35.2 \pm 0.3$ ,  $34.7 \pm 0.3$ , and  $33.7 \pm 0.4^\circ\text{C}$  (mean  $\pm$  SD), respectively. Central temperature did not change significantly in any patient during the cooling or rewarming period. Significant changes occurred during cooling and rewarming in adductor pollicis temperature and twitch tension (table 1) and in subcutaneous tissue and thenar skin temperatures,  $3.3 \pm 0.7$  and  $6.6 \pm 0.8^\circ\text{C}$  (mean

TABLE 1. Changes in Adductor Pollicis (AP) Temperature during Local Surface and Central Cooling under Nitrous Oxide/Isoflurane Anesthesia

	Local Surface (n = 15)		Central cooling (n = 10) (results from previous study by Heier <i>et al.</i> ')
	Cooling	Rewarming	
Change in AP temperature (°C)	2.2 ± 2.2	2.5 ± 2.3	1.3 ± 0.4
Change in AP twitch tension (% of control)	13 ± 5	15 ± 9	19 ± 6
% AP twitch tension change/°C change in muscle temperature	6 ± 3 ↓	5 ± 2 ↑	14 ± 6*

Values are mean ± SD. Arrows indicate directional change twitch tension.

\* Statistically significant difference between local and general cooling.

± SD), respectively. These changes were similar during cooling and rewarming. The reduction in twitch tension/°C reduction in muscle temperature in this study during local surface cooling was 6 ± 3%/°C (mean ± SD).

A significant temperature gradient between skin and subcutaneous tissue, 4.4 ± 0.9°C (mean ± SD) and between subcutaneous tissue and adductor pollicis muscle, 1.1 ± 0.6°C (mean ± SD), was observed during cooling and rewarming in all patients. The temperature gradients were similar during cooling and rewarming.

Figure 1 shows the effect of local cooling and rewarming in one patient. No significant effect on twitch tension was observed during either cooling or rewarming in two patients. In the remaining 13 patients, there was a significant correlation between adductor pollicis temperature and twitch tension during cooling and rewarming (cor-

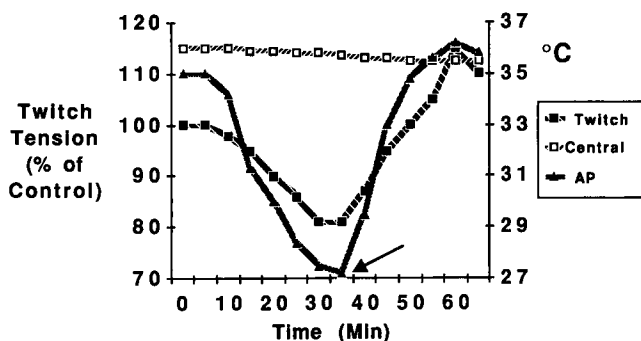


FIG. 1. Changes in central and adductor pollicis (AP) temperatures and adductor pollicis twitch tension in one patient undergoing local cooling and rewarming of the thenar eminence during isoflurane anesthesia. Arrow indicates when rewarming started. There was a significant linear relationship between twitch tension and muscle temperature during cooling and rewarming. Twitch tension decreased 19% when adductor pollicis temperature decreased from 35 to 27°C. Central temperature did not change significantly during the cooling period.

relation coefficient range 0.87–0.99,  $P < 0.05$  in all cases). The slopes of the twitch tension/adductor pollicis temperature regression were similar during cooling, 5.6 ± 2.1%/°C (mean ± SD), and rewarming, 4.7 ± 1.9%/°C (mean ± SD). The number of points used in each regression ranged from 6 to 10. Data from the rewarming phase was obtained in only ten of these patients because surgical considerations mandated administration of muscle relaxants to three patients before the study was completed.

The decrease in twitch tension commenced over a wide range of measured muscle temperatures (33–35.5°C) and a consistent temperature threshold for change in twitch tension was not defined.

TOF ratio did not change significantly in any patient during either cooling or rewarming.

PART 2

Central and adductor pollicis temperatures, after the control twitch recording was obtained, but before central cooling started, were 36.5 ± 0.2 and 35.6 ± 0.3°C (mean ± SD), respectively. Central and adductor pollicis temperatures decreased significantly (table 2). The mean maximum difference between central and adductor pollicis temperatures was 0.9 ± 0.2°C (mean ± SD) with the former temperature consistently higher. A significant linear relationship was found between central and adductor pollicis temperatures (central temperature = 0.80 × adductor pollicis temperature + 6.22,  $r = 0.89$ ,  $P < 0.05$ ).

The initial decrease in muscle and central temperatures was not accompanied by a decrease in twitch tension. However, adductor pollicis twitch tension decreased significantly when muscle temperatures were <35.2 ± 0.2°C (mean ± SD) and central temperatures < 36.0 ± 0.1°C (fig. 2). A significant linear relationship was found between central and adductor pollicis temperatures and adductor pollicis twitch tension in each individual (corre-

TABLE 2. Changes in Temperatures and Adductor Pollicis (AP) Twitch Tension during Central Cooling

	Nitrous oxide/fentanyl (n = 5)	Nitrous oxide/isoflurane (n = 10) (results from previous study by Heier <i>et al.</i> ')
AP temperature decrease (°C)	1.5 ± 0.6	1.3 ± 0.4
Central temperature decrease (°C)	1.7 ± 0.5	1.7 ± 0.8
AP twitch tension decrease (% of control)	25 ± 6	19 ± 6
AP twitch tension reduction/°C reduction in muscle temperature	16.4 ± 6	14.1 ± 6

Values are mean ± SD.

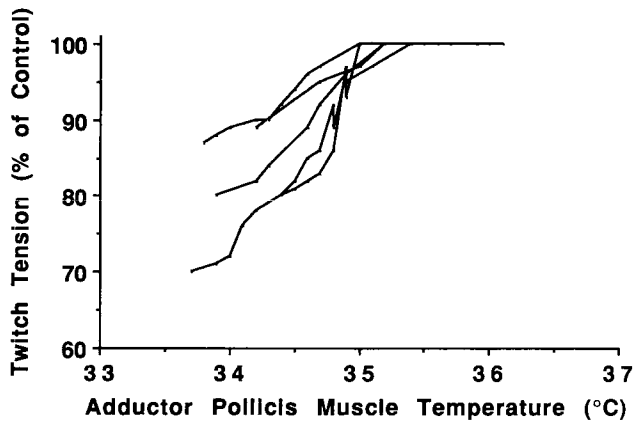


FIG. 2. Effect of systemic cooling on adductor pollicis twitch tension in five patients during nitrous oxide/fentanyl anesthesia. Mean decrease in twitch tension was 16.4%/° C decrease in muscle temperature. The lowest muscle temperature corresponding to a twitch tension = 100% (threshold) was  $35.2 \pm 0.2^\circ \text{C}$  (mean  $\pm$  SD). Each line represents one patient.

lation coefficient between 0.90 and 0.97,  $P < 0.05$ ), with a mean reduction in twitch tension of 16.4%/° C (table 2).

TOF ratio did not change significantly in any patient during active cooling.

### Discussion

The slope of the twitch tension/muscle temperature regression during local surface cooling was less than half of that observed in our previous study during central cooling, despite otherwise similar experimental conditions (6 vs. 14%).<sup>1</sup> This difference may be explained assuming that local surface and central cooling affect adductor pollicis muscle temperature differently. In our previous study, during central cooling the central and adductor pollicis temperatures declined in parallel with a difference of 0.5–1° C between them. Therefore, during central cooling adductor pollicis temperature is largely determined by central temperature. In this situation, it does not matter where in the muscle the thermocouple needle is located because all parts of the muscle will be perfused with cool blood and have similar temperatures.

The adductor pollicis muscle is the deepest muscle in the thenar eminence and is largely covered by other muscles in this region.<sup>7</sup> The only part of the muscle into which a needle thermocouple can be inserted without risk of damage to blood vessels and nerves is the small, superficial part close to the metacarpo-phalangeal joint of the thumb.<sup>§</sup> We observed a temperature gradient between

skin surface, subcutaneous tissue, and muscle during local surface cooling. Therefore, during local surface cooling, the deeper parts of the muscle are likely to remain warmer than the superficial portion in which the thermocouple was inserted. Consequently, the twitch response to local surface cooling appears to be less than that during central cooling probably because with our technique we were unable to adequately measure the average adductor pollicis muscle temperature during local surface cooling conditions.

During local surface cooling, there was a significant linear relationship in each individual patient between observed adductor pollicis temperature and twitch tension, indicating a close relationship between superficial and average muscle temperature. However, the decrease in twitch tension commenced over a wide range of measured adductor pollicis temperatures suggesting that the effect of local surface cooling on the average muscle temperature is unpredictable. The fact that the twitch tension did not change significantly in two patients, despite a change in recorded muscle temperature, is an indication in the same direction. In these patients the twitch tension did not change probably because local cooling did not significantly decrease the average muscle temperature.

In our previous study we found a significant linear relationship between adductor pollicis temperature and twitch tension below a muscle temperature threshold of  $35.3 \pm 0.2^\circ \text{C}$  obtained by central cooling during nitrous oxide/isoflurane anesthesia.<sup>1</sup> The corresponding mean central temperature threshold was  $36 \pm 0.2^\circ \text{C}$ . Twitch tension decreased approximately 14%/° C reduction in muscle temperature below the muscle temperature threshold. In the present study using a different anesthetic (*i.e.*, nitrous oxide/fentanyl) we found that central cooling has a similar effect (table 2). The effect on adductor pollicis twitch tension may result from reduced muscle temperature alone or from a combined effect of reduced muscle temperature and anesthetics used. Because of the similarity of the results obtained with both anesthetic techniques and the known difference in their effect on neuromuscular function,<sup>5</sup> we conclude that the decrease in adductor pollicis twitch tension is due primarily to the temperature decrease.

The close relationship between central and adductor pollicis muscle temperatures during central cooling in the present and our previous study indicates that local surface cooling effects do not contribute significantly to the reduction in muscle temperature in patients during central cooling. Similar results were obtained when patients were cooled spontaneously without active interference with thermoregulation during nitrous oxide/isoflurane anesthesia.<sup>1</sup> The fact that the same relationship between central and adductor pollicis muscle temperatures was observed during active and passive central cooling indicates

§ Lenard Gordon, M.D., Assoc. Clin. Prof., Orthopedic surgery, University of California, San Francisco, personal communication.

that local surface cooling does not contribute significantly to the reduction in adductor pollicis muscle temperature during routine anesthesia. In addition, the adductor pollicis muscle temperature does not decrease when central temperature is maintained throughout the surgical procedure.<sup>1</sup>

In two recent published reports, increased recovery time from atracurium and vecuronium blockade was found with decreasing skin temperature.<sup>8,9</sup> The authors recommended that the arm used for neuromuscular monitoring should be well covered to avoid temperature reduction. While we agree with these authors that local cooling of the hand should be avoided, our results indicate that it is of primary importance to maintain the central temperature, in order to preserve the adductor pollicis muscle temperature.

Our data suggest that patients who cool during anesthesia may have reduced muscle strength in their hands at the end of surgery. We do not know if our results are applicable to other muscle groups in the body. If muscle relaxants are administered, the twitch tension cannot be expected to recover completely when the central body temperature has decreased during anesthesia. However, we did not observe any significant changes in TOF ratio related to the temperature reduction. Therefore, despite cooling of the patient, monitoring the TOF ratio during recovery from a neuromuscular blockade should provide appropriate and useful information.

In conclusion, we have found that the twitch response to central cooling is independent of the anesthetic technique (nitrous oxide/fentanyl *vs.* nitrous oxide/isoflurane), with an approximately 15% decrease in twitch tension/ $^{\circ}$  C reduction in muscle temperature below an adductor pollicis temperature threshold of 35–35.5 $^{\circ}$  C. During local surface cooling conditions, a significant linear relationship between adductor pollicis twitch tension and

measured muscle temperature was observed in each patient during both cooling and rewarming. However, the effect of local surface cooling on the average adductor pollicis muscle temperature was unpredictable and no temperature threshold could be defined.

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